REMARKS

The specification has been amended to correct certain informalities. The Examiner has pointed out discrepancies between the Figures and Sequence Listing with respect to the numbering of residues. The numbers in the Figures are correct and a corrected substitute Sequence Listing will be submitted to correct the discrepancies.

Claims 1-31 are pending. Applicants affirm the election made during a telephone interview with Examiner Spector on April 10, 1995 and request withdrawal and cancellation of claims 13-27 and 29 without prejudice. Additionally, Claims 2, 5, 6, 8 and 10-12 are hereby cancelled and new claims 32-40 have been added. Accordingly, upon acceptance and entry of this amendment into the record, Claims 1, 3, 4, 7, 9 and 32-40 will be pending in this case. Support for the amended claim language and new claims can be found in the specification as a whole and specifically according to the following Table.

Table

Claim No.	New Phrase	Support
1	"human"	Claim 4(a)
	"wherein the amino acid sequence of the ligand consists of amino acid residues 1 to X of **Fig. 8**, where X is residue 153-332.	Claim 6 and Claim 2(a) and Fig. 8
2	"*mpl* ligand"	Claim 1
7	"*mpl* ligand"	Claim 1
9	"substantially homogeneous *mpl* ligand"	Claim 1
	"encoding residues 1 to X of **Fig. 8** where X is 153."	Claim 6
32	Whole Claim "153-166"	Claim 1 and Page 35, line 4
33	Whole Claim "153 to about 157"	Claim 1 and Page 35, line 2
34	Whole Claim "N-terminal methionyl"	Claim 7 and Page 51, line 24

35	Whole Claim	Claim 4
	"covalently modified with polyethylene glycol."	Page 74, lines 30-34 and U.S. Patent No. 4,179,337
36	Whole Claim	Claim 34, Claim 7, Claim 4
37	Whole Claim	Claim 36, Claim 4
	"covalently modified with polyethylene glycol"	Page 74, lines 30-34 U.S. Patent No. 4,179,337
38	Whole Claim	Claim 9
	"nucleic acid molecules are DNA"	Page 25, line 3
39	Whole Claim	Claim 9
	"SPAPPACDLRVLSKLLRDSHVLHSRL"	Figure 7
40	Whole Claim	Claim 9
	"Figure 8 from residue 1 to residue 153"	Claim 6

Accordingly, Applicants submit no new matter has been added. Applicants respectfully request reconsideration of the objections and rejections made in paper no. 6 pursuant to 37 C.F.R. § 1.111 in view of the foregoing amendments and the explanation provided below.

I. Double Patenting Rejections

The Examiner has provisionally rejected the pending claims under a provisional double patenting rejection. Applicants intend to cure this rejection by cancelling certain claims once they have been determined patentable.

The Examiner has also provisionally rejected pending claims under the doctrine of obviousness-type double patenting. Applicants intend to cure this rejection by filing a terminal disclaimer where appropriate.

II. Rejections/Objections Under 35 U.S.C. § 112

The Examiner has rejected original claims 1-12, 28, 30 and 31 under § 112 for the reasons set forth on pages 10-15 of paper no. 6. The original claims have been amended or cancelled rendering many of the Examiners rejections and objections moot. The following explanation attempts to address

the Examiners § 112 concerns for those original claims remaining, as amended.

1. Claims have been amended to remove the term "polypeptide".

2. The term "prepro" or "pro" does not appear in any of the remaining claims.

3. Claims have been amended to define human *mpl* ligand and specifically refer to those amino acid residues found in Figure 8, from residue 1 to X where X ranges from 153 to 332. Applicants demonstrate biological activity for both the full length (hML_{332}) and the "epo-domain" fragment (hML_{153}) in *in vivo* and/or *in vitro* assays (see Figure 12 and its description on page 20, lines 4-26). These forms of the human *mpl* ligand are demonstrated to have comparable biological activity in a cell proliferation assay (H^3-Thymidine incorporation) and a megakaryocytopoiesis assay (platelet $GPII_bIII_a$ quantitation). *In vivo* activity is also demonstrated in a murine platelet rebound assay using human *mpl* ligand. Accordingly, Applicants believe the claims, as amended, are commensurate with the teaching of the specification.

4. Claim 9 has been amended to encompass *mpl* ligands encoded by nucleic acid that hybridize under stringent conditions with nucleic acids encoding the first 153 amino acid residues of human *mpl* ligand. Applicants believe the scope of this claim is commensurate with the teaching of the specification.

5. Claim 4, defining non-immunogenic *mpl* ligands, depends from Claim 1, which in turn specifically defines human *mpl* ligand residues 1 - X of Figure 8 where X is 153-332. These non-immunogenic *mpl* ligands are also defined in Claim 35 (and Claim 37) as specifically containing polyethylene glycol. Applicants enclose a copy of U.S. Patent 4,179,337, entitled "Non-immunogenic polypeptides", which defines polyethylene glycol as a preferred polymer to produce or insure against immunogenicity. This patent is specifically cited on page 74, line 34 and is incorporated by reference on page 102, line 35. Applicants believe the claims, as amended, defining non-immunogenic human *mpl* ligands are commensurate with the scope of teaching in the specification.

Applicants respectfully request reconsideration of the rejection to the pending claims under 35 U.S.C. § 112 in view of the foregoing amendments and explanation thereof.

III. Rejection of Claims 9 and 10 Under 35 U.S.C. § 102(b)

The Examiner has rejected Claims 9 and 10 as being anticipated by the mucin protein disclosed by Girard et al. Specifically, mucin contains the amino acid sequence PTPTPTS which sequence is also found near the carboxyl terminus of human *mpl* ligand (residues 310-316). Applicants have amend Claim 9 to define residues 1-153 of human *mpl*.

Applicants believe this amendment resolves the anticipation issue of Claim 9.

The Examiner is invited to call the undersigned attorney for Applicants if there are any matters that can be expeditiously handled by a telephone interview.

Respectfully submitted,

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